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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/764,415 | 01/23/2004 | Mark William Bodmer | 674525-2009 | 8348 |

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| EXAMINER | |
|---|---|
| BUNNER, BRIDGET E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | |

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/764,415 | BODMER ET AL. | |
| | Examiner | Art Unit | |
| | Bridget E. Bunner | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 November 2004*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-84* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Elections/Restrictions*

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-49 and 83-84, drawn to a method of detecting modulators of Notch or immune signaling, classified in class 435, subclass 4.

II. Claims 50-51, drawn to a modulator of Notch, classification dependent upon structure of modulator.

III. Claims 52-58, drawn to a method of treating a disease or condition comprising administering a modulator of Notch, classified in class 514, subclass 2, for example.

IV. Claim 59, drawn to a particle comprising a protein comprising a Delta DSL domain and at least one Delta EGF domain bound to a particulate support matrix, classified in class 530 subclass 350.

V. Claims 60-64, drawn to a particle comprising a protein comprising a Delta extracellular domain, or an active portion thereof, bound to a particulate support matrix, classified in class 530, subclass 350.

VI. Claims 65-68, drawn to a method of identifying genes which are upregulated in an immune cell, classified in class 435, subclass 6.

VII. Claim 69, drawn to a gene that is upregulated in an immune cell in response to a combination of Notch signaling and immune cell activation, classified in class 536, subclass 23.1.

VIII. Claims 70-78, drawn to an assay for identifying a compound that modulates Notch signaling comprising providing a culture of immune cells, transfecting said cells with a Notch signaling reporter construct, optionally transfecting the cells with a nucleic acid encoding Notch, optionally providing a Notch ligand, exposing the cells to a compound, and determining the difference in signaling, classified in class 435, subclass 6.

IX. Claims 79-82, drawn to an immune cell transfected with a Notch signaling reporter construct and an expression vector encoding Notch, classified in class 435, class 325.

The inventions are distinct, each from the other because of the following reasons:

a. Inventions II, IV, V, VII, and IX are directed to related products. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). The modulator, gene, proteins, and immune cell of Groups II, IV, V, VII, and IX are structurally and functionally diverse from each other. Furthermore, the distinct products require separate, distinct, and non-coextensive searches. As such, it would be burdensome to search the inventions of Groups II, IV, V, VII, and IX together.

b. Inventions I, III, VI, and VIII are directed to related methods. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). Groups I, III, VI, and VIII are different methods requiring different method steps, wherein each is not required, one for another. For example, Invention I requires search and consideration of activating Notch signaling in a cell, contacting the cell with a candidate modulator of Notch or immune signaling, and monitoring Notch signaling, which is not required by the other inventions. Invention III requires search and consideration of administration of a modulator of Notch to treat a disease or condition, which is not required by the other inventions. Invention VI requires search and consideration of identification of genes which are upregulated in an immune cell, which is not required by the other inventions. Invention VIII requires search and consideration of providing a culture of immune cells, transfecting said cells with a Notch signaling reporter construct, optionally transfecting the cells with a nucleic acid encoding Notch, optionally providing a Notch ligand, exposing the cells to a compound, and

determining the difference in signaling, which is not required by the other inventions.

Furthermore, the distinct steps and products require separate, distinct, and non-coextensive searches. As such, it would be burdensome to search the inventions of Groups I, III, VI, and VIII together.

c. Inventions II and I, III are related as product and product of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using the product. See MPEP § 806.05(h). In the instant case, the product claimed can be used in materially different processes, such as cell culture assays.

Additionally, searching the inventions of Groups II and I, III together would impose a serious search burden. The inventions of II and I, III have a separate status in the art as shown by their different classifications. Moreover, the search for a Notch modulator and the methods of use are not coextensive.

d. Inventions VII and VI are related as product and product of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using the product. See MPEP § 806.05(h). In the instant case, the product claimed can be used in materially different processes, such as to produce a protein or in gene therapy.

Additionally, searching the inventions of Groups VII and VI together would impose a serious search burden. The inventions of VII and VI have a separate status in the art as shown by their different classifications. Moreover, the search for an upregulated gene and the methods of use are not coextensive.

e. Inventions IX and VIII are related as product and product of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using the product. See MPEP § 806.05(h). In the instant case, the product claimed can be used in materially different processes, such as in immunotherapeutics or to produce a polypeptide.
Additionally, searching the inventions of Groups IX and VIII together would impose a serious search burden. The inventions of IX and VIII have a separate status in the art as shown by their different classifications. Moreover, the search for an immune cell transfected with a Notch signaling reporter construct and an expression vector encoding Notch and the methods of use are not coextensive.

f. Inventions II and VI/VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions of Groups II and VI/VIII are unrelated product and methods, wherein each is not required, one for another. For example, the product of Invention II cannot be used together with the claimed methods of Inventions VI/VIII because these inventions do not recite the use or production of the product.

g. Inventions IV/V and I/III/VI/VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions of Groups V/VI and I/III/VI/VIII are unrelated products and methods, wherein each is not required, one for another. For example, the products of Inventions IV/V cannot be used together with the claimed methods of Inventions I/III/VI/VIII because these inventions do not recite the use or production of the products.

h. Inventions VII and I/III/VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions of Groups VII and I/III/VIII are unrelated product and methods, wherein each is not required, one for another. For example, the product of Invention VII cannot be used together with the claimed methods of Inventions I/III/VIII because these inventions do not recite the use or production of the product.

i. Inventions IX and I/III/VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions of Groups IX and I/III/VI are unrelated product and methods, wherein each is not required, one for another. For example, the product of Invention IX cannot be used together with the claimed methods of Inventions I/III/VI because these inventions do not recite the use or production of the product.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification and require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

2. This application contains claims directed to the following patentably distinct species: A method of monitoring Notch signaling by monitoring at least one gene, wherein the gene is:

a. an endogenous target gene of Notch signalling

b. CBF-1

c. Hes-1

d. Hes-5

e. E(spl)

f. IL-10

g. CD-23

h. Dlx-1

i. CTLA4

j. CD-4

k. Numb

l. Mastermind

m. Dsh

n. a reporter gene

The species are independent or distinct because each of the genes listed as (a)-(n) have different structural and functional characteristics. The species are independent or distinct because each requires separate, non-coextensive searches. For example, a technical literature search for monitoring the CBF-1gene may not result in relevant art with respect to monitoring the Numb gene.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1 and 13 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an

allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

3. This application contains claims directed to the following patentably distinct species: A second signal that results from activation of a signaling pathway, wherein the signaling pathway specific to cells of the immune system is:

p. a TCR signaling pathway

q. a BCR signaling pathway

r. a TLR signaling pathway

The species are independent or distinct because each of the pathways listed as (p)-(r) involve different signals, cells, and gene/proteins. The species are independent or distinct because each requires separate, non-coextensive searches. For example, a technical literature search for a TCR signaling pathway may not result in relevant art with respect to a TLR signaling pathway.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 13, 20, 22 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

4. This application contains claims directed to the following patentably distinct species: A third signal is a co-stimulus, wherein the co-stimulus is listed in claims 27-28.

The species are independent or distinct because each of the proteins involve different signals, cells, and structural and functional characteristics. The species are independent or distinct because each requires separate, non-coextensive searches. For example, a technical literature search for CD2 may not result in relevant art with respect to cytokines.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 13, 20, 21, 26, and 27 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

5. This application contains claims directed to the following patentably distinct species: A method for detecting Notch signaling wherein Notch signaling is activated by:

s. activating Notch

t. providing a constitutively active truncated Notch

u. providing an active Notch IC domain

The species are independent or distinct because each of the types of Natch activation listed as (s)-(u) involve different mechanisms and genes/proteins. The species are independent or distinct because each requires separate, non-coextensive searches. For example, a technical literature search for a constitutively active truncated Notch may not result in relevant art with respect to an active Notch IC domain.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 1 is generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double

patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

**In addition to the election from one of Inventions I-X, one species from the (a) gene group, (b) signaling pathway group, (c) third signal co-stimulus group, (d) method of activating Notch signaling group must also be chosen to be considered fully responsive.**

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
02 October 2006

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER